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AMENDMENTS TO THE CLAIMS

1. (Currently amended) A compound of formula I:

or a pharmaceutically acceptable salt thereof, wherein:

$$is$$
 R^4 R^4

$$\underbrace{S}_{R^4}
\underbrace{\begin{array}{c} X_2 \\ X_2-X_1 \end{array}}
\underbrace{\begin{array}{c} X_1-S \\ X_1-S \end{array}}
\underbrace{\begin{array}{c} X_2 \\ X_2-X_1 \end{array}}
\underbrace{\begin{array}{c} X_2 \\ X_2-X_1 \end{array}}$$

R¹ is halogen, CN, NO₂, or V_mR;

 Z^1 and Z^3 are each independently CR^Z ; [[, and]]

 Z^2 is CR^1 ;

each occurrence of RZ is independently halogen, CN, NO2, or UnR';

 R^2 is U_nR' ;

X⁴ and X² are each independently CR⁴ or N;

each occurrence of R⁴ is independently halogen, CN, NO₂, or V_mR;

each occurrence of U or V is independently an optionally substituted C_{1-6} alkylidene chain, wherein up to two methylene units of the chain are optionally and independently replaced by -NR-, -S-, -O-, -CS-, $-CO_2$ -, -CO-, -CO-,

-CONR-, -NRCO-, -NRCO₂-, -SO₂NR-, -NRSO₂-, -CONRNR-, -NRCONR-,

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-OCONR-, -NRNR-, -NRSO₂NR-, -SO-, or -SO₂-;

m and n are each independently 0 or 1;

each occurrence of R is independently hydrogen or an optionally substituted C₁₋₆ aliphatic group; and each occurrence of R is independently hydrogen or an optionally substituted C₁₋₆ aliphatic group, a 3-8-membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or R and R , two occurrences of R, or two occurrences of R , are taken together with the atom(s) to which they are bound to form an optionally substituted 3-12 membered saturated, partially unsaturated, or fully unsaturated monocyclic or bicyclic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

 Q^1 is -CO- , SO₂-, or -SO₂NR-;

 R^3 is Q^2 -Ar¹, wherein Q^2 is -(CHR⁶)_q-, where q is 1, 2, or 3,

or R² and Q¹-R³, taken together with the <u>intervening</u> nitrogen atom, form the cyclic

group: $(Y)_s$, where s is 1 or 2, each occurrence of Y is independently, as valency and stability permit, -CO-, -CS-, -SO₂-, -O-, -S-, -NR⁵-, or -C(R⁵)₂-, and R⁵ is U_nR^* ;

 Q^2 -and Q^3 is are each independently a bond or a C_{1-6} alkylidene chain, wherein up to two methylene units of the chain are each optionally and independently replaced by -S-, -O-, -CS-, $-CO_2$ -, $-CO_2$ -, and wherein any carbon atom in the one or more methylene units is optionally substituted with one or two occurrences of R^6 , wherein each

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occurrence of R⁶ is independently halogen, CN, NO₂, or U_nR', or two occurrences of R⁶, or R' and R⁶, taken together with the atoms to which they are bound, form an optionally substituted 3-6-membered cycloalkyl, heterocyclyl, aryl or heteroaryl ring; and

Ar¹ is a 5-8 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from oxygen or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from oxygen or sulfur; wherein Ar¹ is optionally substituted with 0-5 independent occurrences of TR⁷; wherein T is a bond or is a C₁-C₆ alkylidene chain wherein up to two methylene units of T are optionally and independently replaced by –NR-, -S-, -O-, -CS-, -CO₂-,

-OCO-, -CO-, -COCO-, -CONR-, -NRCO-, -NRCO₂-, -SO₂NR-, -NRSO₂-,

-CONRNR-, -NRCONR-, -OCONR-, -NRNR-, -NRSO₂NR-, -SO-, or -SO₂-;

Ar 2 is a 5-8 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; wherein Ar^2 is optionally substituted with 0-5 independent occurrences of TR^7 ; wherein T is a bond or is a C_1 - C_6 alkylidene chain wherein up to two methylene units of T are optionally and independently replaced by -NR-, -S-, -O-, -CS-, $-CO_2$ -, -OCO-, -COCO-, -COCO-, -CONR-, -NRCO-, $-NRCO_2$ -, $-SO_2NR$ -,

-NRSO $_2$ -, -CONRNR-, -NRCONR-, -OCONR-, -NRNR-, -NRSO $_2$ NR-, -SO-, or -SO $_2$ -; and

each occurrence of R⁷ is independently R', halogen, NO₂, or CN; provided that:

I) for compounds described where is $X_2 - X_1$, one or more of, or all of the following conditions apply:

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A) for compounds having the structure:

i) when R¹ is Cl, and R² is CH(CH₃)COOCH₃ or hydrogen, then Q¹ R³ is not CO(unsubstituted phenyl), CO(unsubstituted 2-furyl), or COCH₂(unsubstituted phenyl);

- ii) when R⁴ is hydrogen, R² is hydrogen, and Q⁴ is CO-, then R³ is not:
 - a) phenyl-substituted with 4 O(CH₂)₄₋₇CH₃ or 4 (CH₂)₄₋₇CH₃;
 - b) phenyl substituted with 2 Cl, 4 NO₂, 4-Cl, 2 Br, 3 Br, 3 I, 3-CH₃, 4-OCH₂, 3 NO₂, or 4-I;
 - c) 2,6-OCH₃-phenyl;
 - d) (5-Cl, 3-CH₃, 1-phenyl) pyrazol 4 yl; or
 - e) 4-OnBu-phenyl, CH₂O(2 F phenyl), (CH₂)₂phenyl, furan 2-yl, thiophen-2 yl, 4 CH₃-phenyl, -CH₂O(2-CH₃-phenyl), 3-OCH₃-phenyl, 2 (2,5-dimethoxylphenyl)quinolin-4-yl, -NH-(4-Cl-phenyl), -NH-(3,4-dichlorophenyl), (2-CO₂H, 3 NO₂) phenyl, 3,5-dimethyl-ixoxazol 4-yl, -CH=CH-phenyl, 4 F phenyl, C(CH₂)₂O-(4-Cl-phenyl), NH(3-Cl-phenyl), -NHphenyl, unsubstituted phenyl, 3,4,5-OCH₃-phenyl, 4 NO₂-phenyl, 4-cyclopentoxy-phenyl, -(CH₂)₃phenyl, (tricyclo[3.3.1.13,7]decan 1-yl, -CH₂O-(3-CH₃-phenyl), 3-NO₂-phenyl, -cyclopropyl (4-tert-butyl-phenyl), 2,3-OCH₃-phenyl, 1,3-benzodioxo-5-yl, -CH₂-O-(4-F-phenyl), or 3-Br-phenyl;

iii) when R¹ is hydrogen, R² is hydrogen, and Q¹ is CSNH, then R³ is not 2,3,4,6 tetra O acetyl β-D-glucopyranosyl;

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iv) when R¹-is hydrogen, R² is hydrogen, and Q¹-is SO₂, then R³-is not unsubstituted phenyl, unsubstituted benzyl, unsubstituted naphthyl, phenyl substituted with para-NHCOCH₃, para NH₂, or para CH₃; and

v) when R¹ is hydrogen, R² is -CH₂CH=CH₂, and Q¹ is CO, then R³ is not 4-OCH₃ phenyl, unsubstituted naphthyl, NH (4-OCH₃ phenyl), 3,5-OCH₃-phenyl, CH₂Ophenyl, CH₂-thiophen-2-yl, or CH(phenyl)(CH₂CH₃); and

vi) when R¹ is hydrogen, R² is CH₂CH₃, and Q¹ is CO, then R³ is not 2,4-Cl-phenyl; and

e: \mathbb{R}^2 \mathbb{R}^3 \mathbb{R}^2 \mathbb{R}^3

B) for compounds having the structure:

hydrogen or CH3, and Q1 is CO-, then R3 is not OCH2CH2OCH2phenyl;

II) for compounds described where is X₁-S, one or more of, or al of the following conditions apply:

A) for compounds having the structure:

i) when R³-is Q²-Ar¹-, and Q²-is a bond then Ar¹-is not any one or more of the following: unsubstituted phenyl or phenyl substituted with 2 Br; 2 Cl; 2 I; 2,6-F; 3,5-OCH₃; 3,4,5 OCH₃; 2,4-OCH₃; 3,4-CH₃; 2,5-Cl; 3,4, OCH₃; 2-Cl, 5-NO₂; 3,5-Cl; 3-O(CH₂)₄CH₃, 3-O-n-butyl, 3-CF₃, 3-OCH₃, 3-Br; 3-NO₂; 3-CH₃; 3-O-phenyl; 3-Cl; 4-N(CH₃)₂; 4-N(CH₂CH₃)₂; 4-SO₂N(R²)₂; 4-CN; 4-COOCH₃; 4-C(O)phenyl; 4-phenyl; 4-tert butyl, 4-O-phenyl; 4-O-isopropyl; 4-OCH₃; 4-O-CH₂CH₃; 4-O-n-butyl; 4-Cl; 4-Br; 4-F; 4-CH₃; 4-NO₂; 4-Cl; 3-NO₂, 4-morpholino; 3-NO₂, 2,5-dioxopyrrolidinyl, or 4-piperidinyl; and

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ii) R³ is not any one or more of the following groups:

CH=CH-unsubstituted phenyl, -CH₂(3-NHCOPh-phenyl), -6-bromo-2-(4-ethylphenyl) 4 quinolinyl; -CH₂-pyrrolidine, unsubstituted cyclohexyl, unsubstituted benzyl, unsubstituted furan-2-yl, -CH=CH(3-NO₂-phenyl), -CH₂-naphthyl, unsubstituted naphthyl, unsubstituted thiophene, unsubstituted cyclopropyl, 1,4-benzodioxin, 2-oxo-1-benzopyran, 4-oxo-1-benzopyran, 2-thienyl-quinolin-4-yl, 3-chloro-benzo[b]thiophen-2-yl, 5-Br-(thiophen-2-yl), 5-Cl-(thiophen-2-yl), 5-NO₂ (furan-2-yl), 2,5-Cl-(thiophen-3-yl), -CH=CH-(5-NO₂-thiophen-2-yl), 5-NO₂ (benzothiophen-2-yl), 3-OCH₃ (naphth-2-yl), -CH₂O(2,4-Cl-phenyl), -(CH₂)₂S-phenyl, 2-phenyl-quinolin-4-yl, -CH₂O(4-Cl-phenyl), -CH₂CH₂-3-(4-Cl-phenyl)-1-phenyl-1-H-pyrazol-4-yl, or -CH₂(1,3-dioxoisoindole) [[; and]]

B) for compounds having the structure:

i) when R¹ is Cl, and X₁ is C Cl, then R³ is not NHSO₂-(2-CF₃-phenyl) or NHSO₂ (2,6 dimethoxy phenyl);

ii) when R¹ is CH₃, and X₄ is C CH₃, then R³ is not an optionally substituted indole or optionally substituted dihydroindole; and C) for compounds of general formula I, when Z₄, Z₂ and Z₃ are each CH, R¹ is H, X¹ is CH and X₂ is C COOCH₃, then R³ is not 2 (4 ethyl-phenyl) 6 bromoquinolin 4-yl; and

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III. for compounds described above where so solve is solv

A) when Z¹, Z² and Z³ are each CH, X² is N, X¹ is CH, Q¹ is CONR-, and R² is hydrogen or CH₃, then R³ is not optionally substituted pyridyl, optionally substituted thiazol 4 yl, CH₂pyridyl, benzimidazol 4 yl, quinolin-2-yl, 1 bromo isoquinolin 3 yl, benzthiazol-2-yl, optionally substituted 5,6,7,8-tetrahydro naphthyridin-2-yl, or phenyl substituted with CH₂piperidinyl; and

B) when Z¹, Z² and Z³ are each CH, X² is N, X¹ is CH, Q¹ is SO₂, and R² is hydrogen, then R³ is not phenyl substituted with hydrogen or -COCH₃;

C) when Z^4 , Z^2 and Z^3 are each CH, X_4 is C CO₂H, X^2 is CH, R^2 is hydrogen, and Q^4 is SO₂, then R^3 is not 2-CH₃-phenyl; and

D) when Z¹, Z² and Z³ are each CH, X₁ is CH, X² is N, R² is hydrogen, and Q¹ is CO, then R³ is not 5-methoxy 6 trifluoromethyl 1H-indole.

2-3. (Canceled)

- 4. (Currently amended) The compound of claim $\underline{1}$ [[3]], wherein R^2 is hydrogen, or is U_nR^2 , where n is 1, and U is a C_{1-6} alkylidene chain wherein one or two methylene units are optionally and independently replaced by O, NR, S, or C(O).
- 5. (Currently amended) The compound of claim 1 [[3]], wherein U is -CH₂-, -CH₂CH₂-, -CH₂CH₂-, -CH₂CH₂CH₂-, -CH₂CH₂CH₂-, -CH₂CH₂-, -CH₂CH₂-, -CH₂CH₂CH₂-, -CH₂CH₂CH₂-, -CH₂CH₂CH₂-, -CH₂CH₂CH₂-, -CH₂CH₂CH₂-, -CH₂CH₂CH₂-, -CH₂CH₂CH₂-, -CH₂CH₂-, -CH₂CH₂-, -CH₂CH₂-, -CH₂-, -CH₂-,

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are hydrogen, C₁-C₄alkyl, optionally substituted tetrahydropyranyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, pyridinyl, phenyl, or cyclohexyl, or R and R', taken together with the nitrogen atom to which they are bound, form an optionally substituted 5- or 6-membered heterocyclyl ring.

- 6. (Currently amended) The compound of claim $\underline{1}$ [[3]], wherein Q^1 is -C(O)- or -SO₂NR-.
- 7. (Canceled)
- 8. (Currently amended) The compound of claim 1 [[7]], wherein R⁶ is CH₂OH, CH₂CH₂OH, OH, OMe, OEt, NH₂, NH(Me), NH(Et), N(Me)(Me), CH₂NH₂, CH₂CH₂NH₂, NHCO₂t-butyl, phenyl, cyclopentyl, methyl, ethyl, isopropyl, cyclopropyl, NH(CH₂)₃NH₂, NH(CH₂)₂NH₂, NH(CH₂)₂NHEt, NHCH₂pyridyl, NHSO₂phenyl, NHC(O)CH₂C(O)Ot-butyl, NHC(O)CH₂NH₃, and NHCH₂-imidazol-4-yl.
- 9. (Previously presented) The compound of claim 3, wherein Ar¹ is:

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wherein t is 0, 1, 2, 3, 4 or 5, and wherein any Ar^1 is bonded to Q^2 through any substitutable carbon atom, and wherein one or more hydrogen atoms on any substitutable carbon atom is substituted with one or more independent occurrences of TR^7 .

- 10. (Previously presented) The compound of claim 9, wherein Ar¹ is **a, e, i, k, cc, jj,** or **pp**.
- 11. (Original) The compound of claim 9, wherein T is a bond or is an optionally substituted C_{1-6} alkylidene chain wherein one or two methylene units are optionally and independently replaced by -O-, -NR-, -S-, -SO₂-, -COO-, -CO-, -OSO₂-, -NRSO₂, -CONR-, or -SO₂NR-, and R⁷ is R' or halogen.
- 12. (Original) The compound of claim 9, wherein each occurrence of TR^7 is independently -C₁₋₃alkyl, -OR', -SR', -CF₃, -OCF₃, -SCF₃, -F, -Cl, I, -Br, -COOR', -COR', -O(CH₂)₄N(R)(R'), -O(CH₂)₃N(R)(R'), -O(CH₂)₂N(R)(R'), -O(CH₂)N(R)(R'), -O(CH₂)₄CON(R)(R'), -O(CH₂)₃CON(R)(R'), -O(CH₂)₂CON(R)(R'), -O(CH₂)₂CON(R)(R'), -C(CH₂)₃OR', -(CH₂)₃OR', -(CH₂)₂OR', -CH₂OR', optionally substituted phenyl or benzyl, -N(R)(R'), -(CH₂)₄N(R)(R'),

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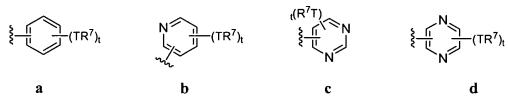
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- $(CH_2)_3N(R)(R')$, - $(CH_2)_2N(R)(R')$, - $(CH_2)N(R)(R')$, or $SO_2N(R)(R')$, $NRSO_2R'$, CON(R)(R'), or $-OSO_2R'$.

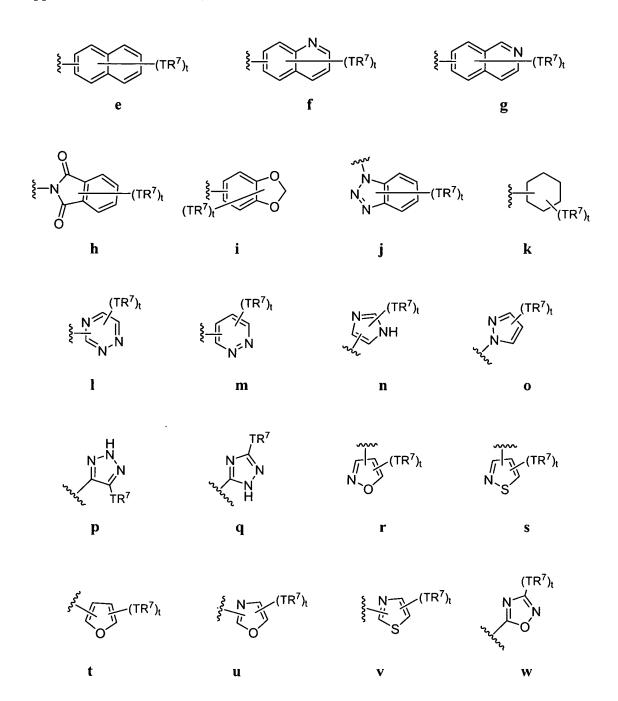
13. (Canceled)

- 14. (Currently amended) The compound of claim $\underline{1}$ [[13]], wherein Q^3 is a direct bond, or is -(CHR⁶)_q-, -(CHR⁶)_qO-, -(CHR⁶)_qS-, -(CHR⁶)_qS(O)₂-, -(CHR⁶)_qS(O)-, -(CHR⁶)_qNR-, or -(CHR⁶)_qC(O)-, wherein q is 0, 1, 2, or 3, and R⁶ is R', -N(R)(R'), -(CH₂)₁₋₄N(R)(R'), -OR', -(CH₂)₁₋₄OR', -NR(CH₂)₁₋₄N(R)(R'), -NR(CH₂)₁₋₄SO₂R', -NR(CH₂)₁₋₄COOR', or -NR(CH₂)₁₋₄COR', or two occurrences of R⁶, taken together with the atoms to which they are bound, form an optionally substituted 3-6-membered saturated, partially unsaturated, or fully unsaturated ring.
- 15. (Original) The compound of claim 14, wherein R⁶ is CH₂OH, CH₂CH₂OH, OH, OMe, OEt, NH₂, NH(Me), NH(Et), N(Me)(Me), CH₂NH₂, CH₂CH₂NH₂, NHCO₂t-butyl, phenyl, cyclopentyl, methyl, ethyl, isopropyl, cyclopropyl, NH(CH₂)₃NH₂, NH(CH₂)₂NHEt, NHCH₂pyridyl, NHSO₂phenyl, NHC(O)CH₂C(O)Ot-butyl, NHC(O)CH₂NH₃, and NHCH₂-imidazol-4-yl.
- 16. (Currently amended) The compound of claim $\underline{1}$ [[13]], wherein Ar² is:



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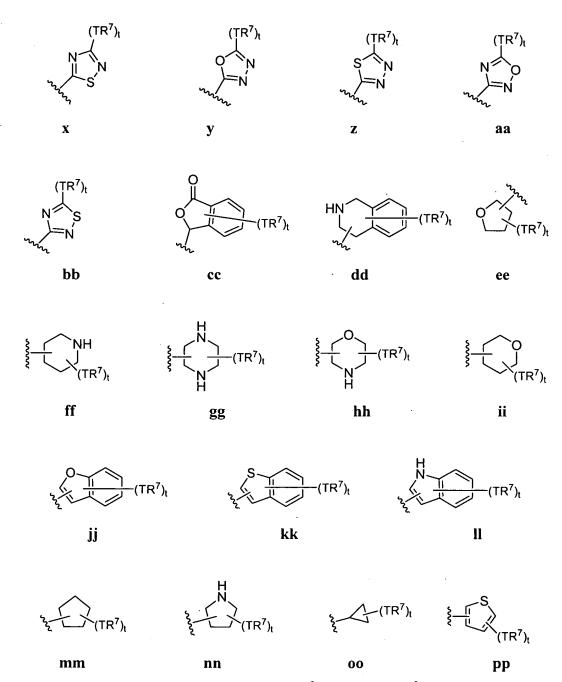
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wherein t is 0, 1, 2, 3, 4 or 5, and wherein any Ar² is bonded to Q³ through any substitutable nitrogen or carbon atom, and wherein one or more hydrogen atoms on any

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substitutable nitrogen or carbon atom is substituted with one or more independent occurrences of TR⁷.

- 17. (Original) The compound of claim 16, wherein Ar² is a, b, e, g, h, i, j, k, n, r, cc, dd, ff, jj, ll, or pp.
- 18. (Original) The compound of claim 16, wherein T is a bond or is an optionally substituted C_{1-6} alkylidene chain wherein one or two methylene units are optionally and independently replaced by -O-, -NR-, -S-, -SO₂-, -COO-, -CO-, -OSO₂-, -NRSO₂, -CONR-, or -SO₂NR-, and R⁷ is R' or halogen.
- 19. (Original) The compound of claim 16, wherein each occurrence of TR^7 is independently $-C_{1-3}$ alkyl, -OR', -SR', $-CF_3$, $-OCF_3$, $-SCF_3$, -F, -Cl, I, -Br, -COOR', -COR', $-O(CH_2)_4N(R)(R')$, $-O(CH_2)_3N(R)(R')$, $-O(CH_2)_2N(R)(R')$, $-O(CH_2)_4CON(R)(R')$, $-O(CH_2)_3CON(R)(R')$, $-O(CH_2)_2CON(R)(R')$, $-O(CH_2)_2CON(R)(R')$, $-O(CH_2)_2CON(R)(R')$, $-O(CH_2)_2CON(R)(R')$, $-C(CH_2)_3CON(R)(R')$, $-C(CH_2)_4OR'$, $-C(CH_2)_3OR'$, $-C(CH_2)_2OR'$, $-CCH_2OR'$, optionally substituted phenyl or benzyl, -N(R)(R'), $-(CH_2)_4N(R)(R')$, $-(CH_2)_3N(R)(R')$, $-(CH_2)_2N(R)(R')$, $-(CH_2)_2N(R)(R')$, or $-OSO_2R'$.
- 20. (Currently amended) The compound of claim <u>1</u> [[13]], wherein R⁵ is hydrogen, (CH₂)₃OR', (CH₂)₂OR', (CH₂)OR', (CH₂)₃N(R')₂, (CH₂)₂N(R')₂, (CH₂)N(R')₂, or C₁. ₄aliphatic.
- 21-22. (Canceled)

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- 23. (Original) The compound of claim 1, wherein each occurrence of R^1 is independently hydrogen, halogen, optionally substituted C_1 - C_4 aliphatic, OR, SR, or $N(R)_2$.
- 24. (Previously presented) The compound of claim 23, wherein each occurrence of R¹ is independently hydrogen, halogen, -CH₃, -CH₂CH₃, -OH, -OCH₃, -SCH₃, -NH₂, -N(CH₃)₂, -N(CH₂CH₃)₂, -NH(CH₂)₂NHCH₃, -NH(cyclopropyl), -NH(CH₂)cyclopropyl, or -NH(CH₂)₂N(CH₃)₂.
- 25. (Original) The compound of claim 1, wherein each occurrence of R^Z is independently hydrogen, halogen, C₁-C₄aliphatic, OH, OR', or N(R)(R').
- 26. (Original) The compound of claim 25, wherein each occurrence of R^Z is independently hydrogen, halogen, Me, OH, OMe, NH₂, or N(Me)₂.
- 27. (Original) The compound of claim 1, wherein R⁴ groups are each independently hydrogen, C₁₋₆aliphatic, CN, COR, C(=O)OR, C(=O)N(R)₂, or halogen.
- 28. (Previously presented) The compound of claim 1, wherein one occurrence of R⁴ is CN and compounds have the general structure II-a:

$$\begin{array}{c|c}
R^1 \\
N \\
Z^1 \\
Z^2 \\
Z^3
\end{array}$$

$$\begin{array}{c|c}
R^2 \\
N \\
Q^1
\end{array}$$

$$\begin{array}{c|c}
R^3 \\
CN
\end{array}$$

II-a.

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29. (Previously presented) The compound of claim 1, wherein R⁴ is hydrogen and compounds have the general structure **III-a**:

$$R^1$$
 Z^1
 Z^2
 Z^3
 S
 N
 Q^1
 R^3
III-a.

30. (Previously presented) The compound of claim 1, wherein one occurrence of R⁴ is hydrogen and the other occurrence of R⁴ is -COOR and compounds have the general structure **VI-a**:

31. (Previously presented) The compound of claim 1, wherein R⁴ is hydrogen and compounds have the general structure VII-a:

$$\begin{array}{c|c}
R^1 \\
N \\
Z^1 \\
Z^2 \\
Z^3
\end{array}$$

$$\begin{array}{c|c}
N \\
N \\
N \\
Q^1
\end{array}$$

$$\begin{array}{c|c}
R^2 \\
N \\
N \\
Q^1
\end{array}$$

$$\begin{array}{c|c}
R^3 \\
\end{array}$$
VIII-a.

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32. (Previously presented) The compound of claim 1, wherein one occurrence of R^4 is hydrogen and the other occurrence of R^4 is C(=O)OR and compounds have the general structure **X-a**:

$$\begin{array}{c|c}
R^1 \\
N \\
Z^1 \\
Z^2 \\
Z^3 \\
S \\
R^4
\end{array}$$
 $\begin{array}{c}
C \\
R^2 \\
N \\
Q^1
\end{array}$
 $\begin{array}{c}
R^3 \\
X-a.
\end{array}$

33. (Previously presented) The compound of claim 1, wherein R⁴ is hydrogen and compounds have the general structure **XI-a**:

34. (Previously presented) The compound of claim 9, wherein Q^1 is -CO-, Q^2 is CHR⁶, q is 1 2, or 3, and compounds have one of formulas XIV, XV, or XVI:

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35. (Previously presented) The compound of claim 9, wherein Q^1 is -CO-, Q^2 is CHR⁶, q is 1, 2 or 3, and compounds have one of formulas **XVII**, **XVIII**, or **XIX**:

- 36. (Previously presented) The compound of claims 34 or 35, wherein compound variables are selected from one of more of the following groups:
- a) each occurrence of R^1 is independently hydrogen, halogen, optionally substituted C_1 - C_4 aliphatic, OR, SR, or $N(R)_2$;
- b) each occurrence of R¹ is independently hydrogen, halogen, -CH₃, -CH₂CH₃, -OH, -OCH₃, -SCH₃, -NH₂, -N(CH₃)₂, -N(CH₂CH₃)₂, -NH(CH₂)₂NHCH₃, -NH(cyclopropyl), -NH(CH₂)cyclopropyl, or -NH(CH₂)₂N(CH₃)₂;

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- c) each occurrence of R^Z is independently hydrogen, halogen, optionally substituted C_1 - C_4 aliphatic, OH, O(R'), or N(R)(R');
- d) each occurrence of R^Z is independently hydrogen, halogen, Me, OH, OMe, NH₂, or N(Me)₂;
 - e) R² is hydrogen, or is U_nR', where n is 1, and U is-CH₂-, -CH₂CH₂-,
- -CH₂CH₂CH₂-, -CH₂CH₂CH₂-, -CH₂O-, -CH₂S-, -CH₂NR-, -CH₂CH₂O-, -CH₂CH₂S-
- , -CH₂CH₂NR-, -CH₂CH₂CH₂O-, -CH₂CH₂CH₂S-, -CH₂CH₂CH₂NR-,
- -CH₂CH₂OCH₂CH₂-, -(CH₂)₄NHCH₂-, -(CH₂)₃NHCH₂CH₂-, or
- -CH₂CH₂NHCH₂CH₂-, and R' groups are hydrogen, C₁-C₄alkyl, optionally substituted tetrahydropyranyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, pyridinyl, phenyl, or cyclohexyl, or R and R', taken together with the nitrogen atom to which they are bound, form an optionally substituted 5- or 6-membered heterocyclyl ring;
- f) each occurrence of R⁴ is independently hydrogen, C₁₋₆aliphatic, CN, COR, COOR, CON(R)₂, or halogen;
 - g) q is 1, 2, or 3;
- h) R⁶ is R', -N(R)(R'), -(CH₂)₁₋₄N(R)(R'), -OR', -(CH₂)₁₋₄OR', -NR(CH₂)₁₋₄ 4N(R)(R'), -NR(CH₂)₁₋₄SO₂R', -NR(CH₂)₁₋₄COOR', or -NR(CH₂)₁₋₄COR', or two occurrences of R⁶, taken together with the atoms to which they are bound, form an optionally substituted 3-6-membered saturated, partially unsaturated, or fully unsaturated ring;
- i) R⁶ is CH₂OH, CH₂CH₂OH, OH, OMe, OEt, NH₂, NH(Me), NH(Et), N(Me)(Me), CH₂NH₂, CH₂CH₂NH₂, NHCO₂t-butyl, phenyl, cyclopentyl, methyl, ethyl, isopropyl, cyclopropyl, NH(CH₂)₃NH₂, NH(CH₂)₂NH₂, NH(CH₂)₂NHEt, NHCH₂pyridyl, NHSO₂phenyl, NHC(O)CH₂C(O)Ot-butyl, NHC(O)CH₂NH₃, and NHCH₂-imidazol-4-yl;
- j) Ar¹ is ring **a**, **e**, **i**, **k**, **cc**, **jj**, or **pp** wherein t is 0, 1, 2, or 3, and T is a bond or is an optionally substituted C_{1-6} alkylidene chain wherein one or two methylene units are

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optionally and independently replaced by -O-, -NR-, -S-, $-SO_2$ -, -COO-, -CO-, $-OSO_2$ -, $-NRSO_2$, -CONR-, or

-SO₂NR-, and R⁷ is R' or halogen; or

- k) Ar^1 is ring **a**, **e**, **i**, **k**, **cc**, **jj**, or **pp** wherein t is 0, 1, 2, or 3, and each occurrence of TR^7 is independently $-C_{1.3}$ alkyl, -OR', -SR', $-CF_3$, $-OCF_3$, $-SCF_3$, -F, -Cl, I, -Br, -COOR', -COR', $-O(CH_2)_4N(R)(R')$, $-O(CH_2)_3N(R)(R')$, $-O(CH_2)_2N(R)(R')$, $-O(CH_2)_4CON(R)(R')$, $-O(CH_2)_3CON(R)(R')$, $-O(CH_2)_2CON(R)(R')$, $-O(CH_2)_2CON(R)(R')$, $-O(CH_2)_3CON(R)(R')$, $-O(CH_2)_3CON(R)$, $-O(CH_2$
- 37. (Previously presented) The compound of claim 34 or 35, q is 1, and Ar¹ is optionally substituted phenyl and compounds of general formula **XIV-A** through **XIX-A** are provided:

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wherein:

each occurrence of R¹ is hydrogen;

each occurrence of RZ is hydrogen;

R² is hydrogen, or is U_nR', where n is 1, and U is-CH₂-, -CH₂CH₂-,

-CH₂CH₂CH₂-, -CH₂CH₂CH₂CH₂-, -CH₂O-, -CH₂S-, -CH₂NR-, -CH₂CH₂O-, -CH₂CH₂S-

, -CH₂CH₂NR-, -CH₂CH₂CH₂O-, -CH₂CH₂CH₂S-, -CH₂CH₂CH₂NR-,

-(CH₂)₄NHCH₂-, -(CH₂)₃NHCH₂CH₂-, or -CH₂CH₂NHCH₂CH₂-, and R' groups are hydrogen, C₁-C₄alkyl, optionally substituted tetrahydropyranyl, pyrrolidinyl, piperidinyl,

piperazinyl, morpholinyl, thiomorpholinyl, pyridinyl, phenyl, or cyclohexyl, or R and R',

taken together with the nitrogen atom to which they are bound, form an optionally

substituted 5- or 6-membered heterocyclyl ring;

each occurrence of R⁴ is independently hydrogen, C₁₋₆aliphatic, CN, COR, CON, CON(R)₂, or halogen;

 R^6 is R', -N(R)(R'), $-(CH_2)_{1-4}N(R)(R')$, -OR', $-(CH_2)_{1-4}OR'$,

 $-NR(CH_2)_{1-4}N(R)(R')$, $-NR(CH_2)_{1-4}SO_2R'$, $-NR(CH_2)_{1-4}COOR'$, or

-NR(CH₂)₁₋₄COR'; and

t is 0, 1, 2, or 3, and each occurrence of TR^7 is independently $-C_{1-3}$ alkyl, -OR', -SR', $-CF_3$, $-OCF_3$, $-SCF_3$, -F, -Cl, I, -Br, -COOR', -COR', $-O(CH_2)_4N(R)(R')$, $-O(CH_2)_3N(R)(R')$, $-O(CH_2)_2N(R)(R')$, $-O(CH_2)N(R)(R')$, $-O(CH_2)_4CON(R)(R')$,

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 $-O(CH_2)_3CON(R)(R')$, $-O(CH_2)_2CON(R)(R')$, $-O(CH_2)CON(R)(R')$, -C(O)N(R)(R'), -(CH_2)₄OR', -(CH_2)₃OR', -(CH_2)₂OR', - CH_2 OR', optionally substituted phenyl or benzyl, -N(R)(R'), $-(CH_2)_4N(R)(R')$, $-(CH_2)_3N(R)(R')$, $-(CH_2)_2N(R)(R')$, -(CH₂)N(R)(R'), -SO₂N(R)(R'), -NRSO₂R', -CON(R)(R'), or -OSO₂R'.

(Previously presented) The compound of claim 16, wherein R² and Q¹-R³, taken 38. together with the atoms to which they are bound form a 5-membered cyclic group, and compounds have the general formula XX through XXV:

XXIV XXV.

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39. (Previously presented) The compound of claim 16, R² and Q¹-R³, taken together with the atoms to which they are bound form a 5-membered cyclic group, and compounds have the general formula **XXVI** through **XXXI**:

$$\begin{array}{c|cccc}
R^1 & R^2 & O & Q^3 - Ar^2 \\
R^1 & S & N & N - R^5 \\
R^2 & N & R^4 & O
\end{array}$$
XXVI

 $\begin{array}{c|cccc}
R^1 & R^2 & O & Q^3 - Ar^2 \\
R^1 & S & N & N - R^5 \\
R^2 & N & R^4 & S
\end{array}$ XXVII

 R^1 R^2 Q^3-Ar^2 R^1 R^2 Q^3-Ar^2

 R^1 R^2 Q^3-Ar^2 N N N N N

XXVIII

XXIX

$$\begin{array}{c|cccc}
R^1 & R^2 & O & Q^3 - Ar^2 \\
R^1 & N & N & N - R^5 \\
R^2 & S & R^4 & S
\end{array}$$
XXXI.

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40. (Previously presented) The compound of claim 16, wherein R² and Q¹-R³, taken together with the atoms to which they are bound form a 6-membered cyclic group, and compounds have the general formula **XXXII** through **XXXVII**:

wherein W is O, NR⁵, or CHR⁵.

- 41. (Original) The compound of claims 38, 39 or 40, wherein compound variables are selected from one of more of the following groups:
- a) each occurrence of R^1 is independently hydrogen, halogen, optionally substituted C_1 - C_4 aliphatic, OR, SR, or $N(R)_2$;

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- b) each occurrence of R^Z is independently hydrogen, halogen, optionally substituted C_1 - C_4 aliphatic, OH, OR' or N(R)(R');
- c) each occurrence of R⁴ is independently hydrogen, C₁₋₆aliphatic, CN, COR, CON(R)₂, or halogen;
- d) R⁵ is hydrogen, (CH₂)₃OR', (CH₂)₂OR', (CH₂)OR', (CH₂)₃N(R')₂, (CH₂)₂N(R')₂, (CH₂)N(R')₂, or C₁₋₄aliphatic;
- e) Q^3 is a direct bond, or is -(CHR⁶)_q-, -(CHR⁶)_qO-, -(CHR⁶)_qS-, -(CHR⁶)_qS(O)₂-, -(CHR⁶)_qS(O)-, -(CHR⁶)_qNR-, or -(CHR⁶)_qC(O)-, wherein q is 0, 1, 2, or 3; and
- f) Ar^2 is ring **a**, **b**, **e**, **g**, **h**, **i**, **j**, **k**, **n**, **r**, **cc**, **dd**, **ff**, **jj**, **ll**, or **pp**, wherein t is 0, 1, 2, or 3, and T is a bond or is an optionally substituted C_{1-6} alkylidene chain wherein one or two methylene units are optionally and independently replaced by $-O_{-}$, $-NR_{-}$, $-S_{-}$, $-SO_{2-}$, $-COO_{-}$, $-CO_{-}$, $-OSO_{2-}$, $-NRSO_{2}$, $-CONR_{-}$, or $-SO_{2}NR_{-}$, and R^{7} is R^{7} or halogen.
- 42. (Previously presented) The compound of claims 38, 39 or 40, wherein compound variables are selected from one of more of the following groups:
- a) each occurrence of R¹ is independently hydrogen, halogen, -CH₃, -CH₂CH₃, -OH, -OCH₃, -SCH₃, -NH₂, -N(CH₃)₂, -N(CH₂CH₃)₂, NH(CH₂)₂NHCH₃, NH(cyclopropyl), NH(CH₂)cyclopropyl, or NH(CH₂)₂N(CH₃)₂;
- b) each occurrence of R^Z is independently hydrogen, halogen, Me, OH, OMe, NH₂, or N(Me)₂;
- c) each occurrence of R⁴ is independently hydrogen, C₁₋₆aliphatic, CN, COR, CON, CON(R)₂, or halogen;
- d) R⁵ is hydrogen, (CH₂)₃OR', (CH₂)₂OR', (CH₂)OR', (CH₂)₃N(R')₂, (CH₂)₂N(R')₂, (CH₂)N(R')₂, or C₁₋₄aliphatic;
- e) Q^3 is a direct bond, or is -(CHR⁶)_q-, -(CHR⁶)_qO-, -(CHR⁶)_qS-, -(CHR⁶)_qS(O)₂-, -(CHR⁶)_qS(O)-, -(CHR⁶)_qNR-, or -(CHR⁶)_qC(O)-, wherein q is 0, 1, 2, or 3; and

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f) Ar^2 is ring **a, b, e, g, h, i, j, k, n, r, cc, dd, ff, jj, ll**, or **pp**, wherein t is 0, 1, 2, or 3, and each occurrence of TR^7 is independently $-C_{1-3}$ alkyl, -OR', -SR', $-CF_3$, $-OCF_3$, $-SCF_3$, -F, -Cl, I, -Br, -COOR', -COR', $-O(CH_2)_4N(R)(R')$, $-O(CH_2)_3N(R)(R')$, $-O(CH_2)_2N(R)(R')$, $-O(CH_2)N(R)(R')$, $-O(CH_2)_4CON(R)(R')$, $-O(CH_2)_3CON(R)(R')$, $-O(CH_2)_2CON(R)(R')$, $-O(CH_2)_2CON(R)(R')$, $-O(CH_2)_3CON(R)(R')$, $-C(CH_2)_3OR'$, $-(CH_2)_2OR'$, $-CH_2OR'$, optionally substituted phenyl or benzyl, -N(R)(R'), $-(CH_2)_4N(R)(R')$, $-(CH_2)_3N(R)(R')$, $-(CH_2)_2N(R)(R')$, $-(CH_2)_2N($

43. (Previously presented) The compound of claims 38, 39 or 40, wherein Ar² is optionally substituted phenyl and compounds of general formula **XX-A**, through **XXXVII** are provided:

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$$R^1$$
 R^2
 R^3
 R^4
 R^4
 R^5
 R^5

XXIV-A

$$R^1$$
 R^2
 R^3
 R^4
 R^5
 R^5
 R^4
 R^5

XXV-A

XXVI-A

$$R^1$$
 R^2
 R^4
 $N - R^5$
 R^4
 $N - R^5$

XXVII-A

$$R^1$$
 R^2
 Q^3
 Q^3

XXVIII-A

$$R^1$$
 R^2
 R^2
 R^3
 R^4
 R^2
 R^4
 R^5
 R^5

XXIX-A

$$R^1$$
 R^2
 R^4
 R^5
 R^5
 R^5

XXX-A

$$R^1$$
 R^2
 R^2
 R^3
 R^5
 R^5

XXXI-A

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 R^{1} R^{2} R^{4} R^{2} R^{4} R^{5} R^{4} R^{5} R^{4} R^{5} R^{4} R^{5}

XXXII-A

XXXIII-A

$$\begin{array}{c|c}
R^1 & R^2 & Q^3 & (TR^7)_{t} \\
R^1 & R^2 & N & N-R^5 \\
R^2 & S & R^4 & O
\end{array}$$

XXXIV-A

XXXV-A

$$R^{1}$$
 R^{2}
 R^{2}
 R^{4}
 R^{5}
 R^{5}

 R^{1} R^{2} R^{2} R^{3} R^{5} R^{4}

XXXVI-A

XXXVII-A.

44. (Previously presented) The compound of claim 43, wherein compound variables are selected from:

each occurrence of R^1 is hydrogen;

each occurrence of RZ is hydrogen;

each occurrence of R^4 is independently hydrogen, $C_{1\text{-}6}$ aliphatic, CN, COR, COOR, CON(R)₂, or halogen;

 R^5 is hydrogen, $(CH_2)_3OR$ ', $(CH_2)_2OR$ ', $(CH_2)OR$ ', $(CH_2)_3N(R')_2$, $(CH_2)_2N(R')_2$, $(CH_2)N(R')_2$, or C_{1-4} aliphatic;

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 $Q^{3} \text{ is a direct bond, or is -}(CHR^{6})_{q}\text{-}, -(CHR^{6})_{q}\text{O-}, -(CHR^{6})_{q}\text{S-}, -(CHR^{6})_{q}\text{S}(O)_{2}\text{-}, -(CHR^{6})_{q}\text{S}(O)_{2}\text{-}, -(CHR^{6})_{q}\text{N}R-, or -}(CHR^{6})_{q}\text{C}(O)\text{-}, wherein q is 0, 1, 2, or 3; and t is 0, 1, 2, or 3, and each occurrence of TR⁷ is independently -C₁₋₃alkyl, -OR', -SR', -CF₃, -OCF₃, -SCF₃, -F, -Cl, I, -Br, -COOR', -COR', -O(CH₂)₄N(R)(R'), -O(CH₂)₃N(R)(R'), -O(CH₂)₂N(R)(R'), -O(CH₂)₃N(R)(R'), -O(CH₂)₂N(R)(R'), -O(CH₂)₃N(R)(R'), -O(CH₂)₄CON(R)(R'),$

 $-O(CH_2)_3CON(R)(R'), -O(CH_2)_2CON(R)(R'), -O(CH_2)CON(R)(R'), -C(O)N(R)(R'), -C(O)N(R'), -C(O)N(R'),$

 $(CH_2)_4OR'$, $-(CH_2)_3OR'$, $-(CH_2)_2OR'$, $-CH_2OR'$, optionally substituted phenyl or benzyl, -N(R)(R'), $-(CH_2)_4N(R)(R')$, $-(CH_2)_3N(R)(R')$, $-(CH_2)_2N(R)(R')$,

- $(CH_2)N(R)(R')$, - $SO_2N(R)(R')$, - $NRSO_2R'$, -CON(R)(R'), or - OSO_2R' .

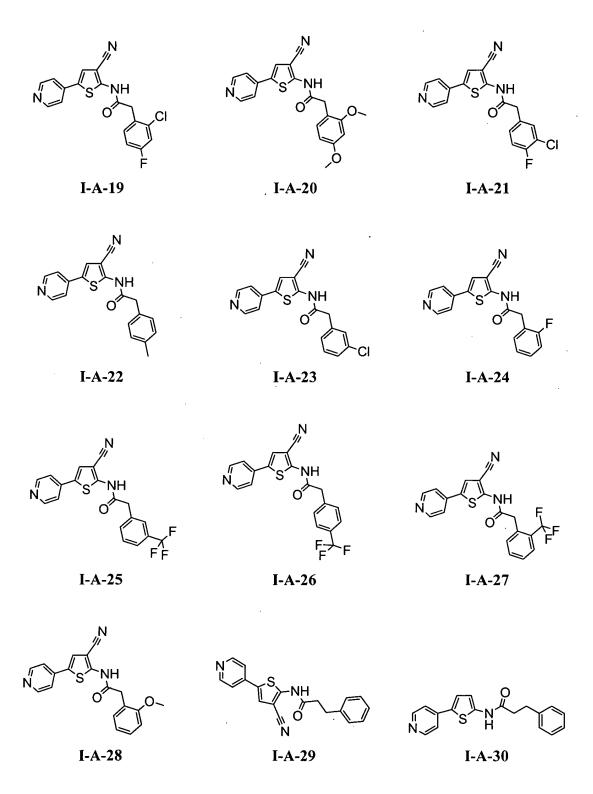
45. (Currently amended) The compound of claim 1, having one of the structures:

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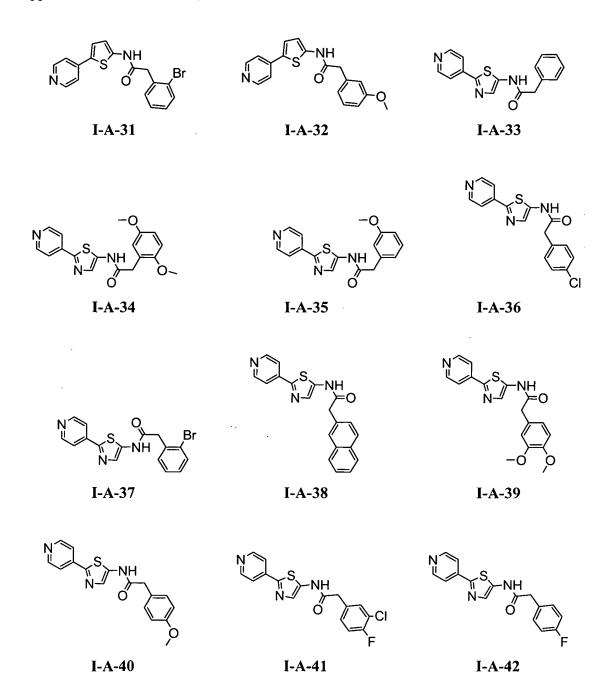
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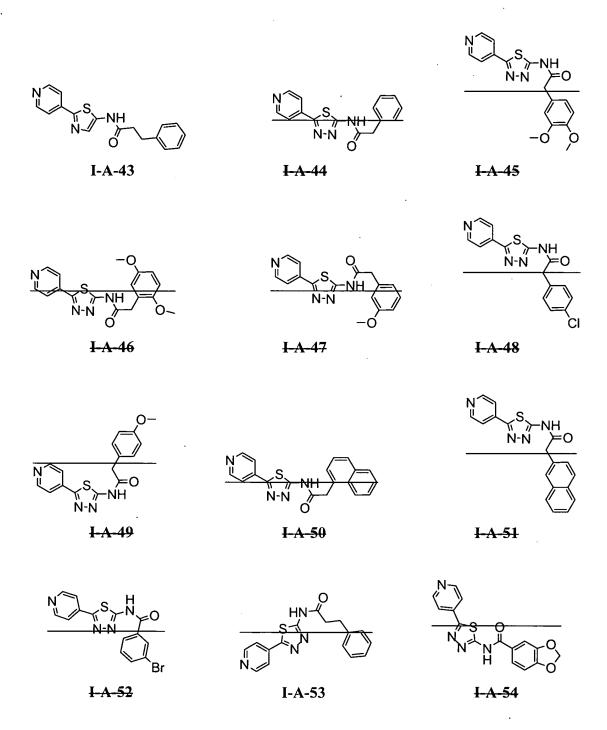
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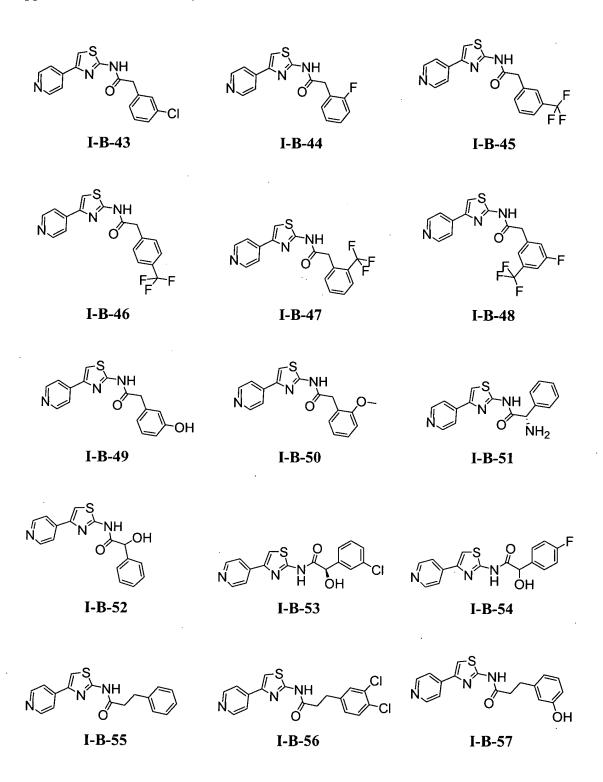
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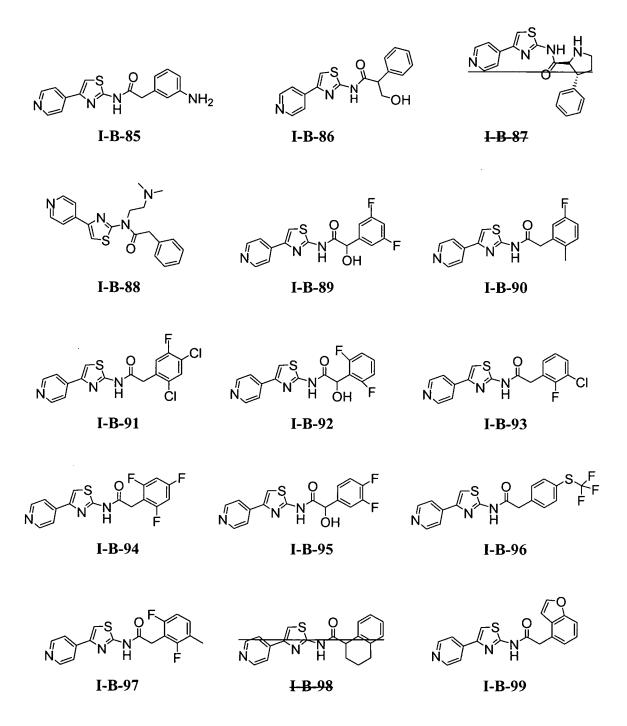
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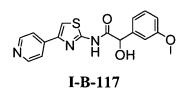
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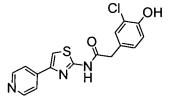
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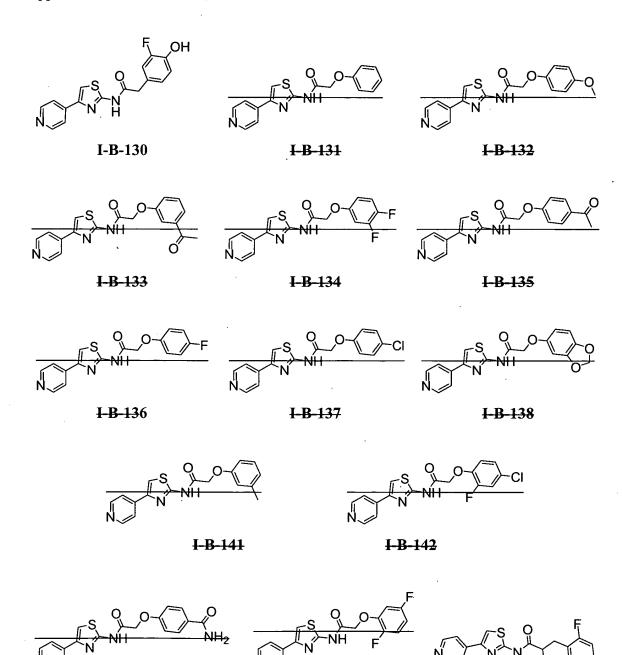
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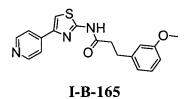
I-B-144

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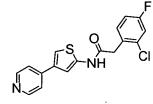
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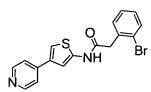
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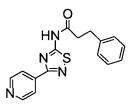
I-B-248



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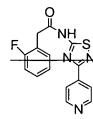
I-B-251

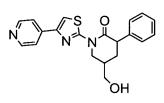


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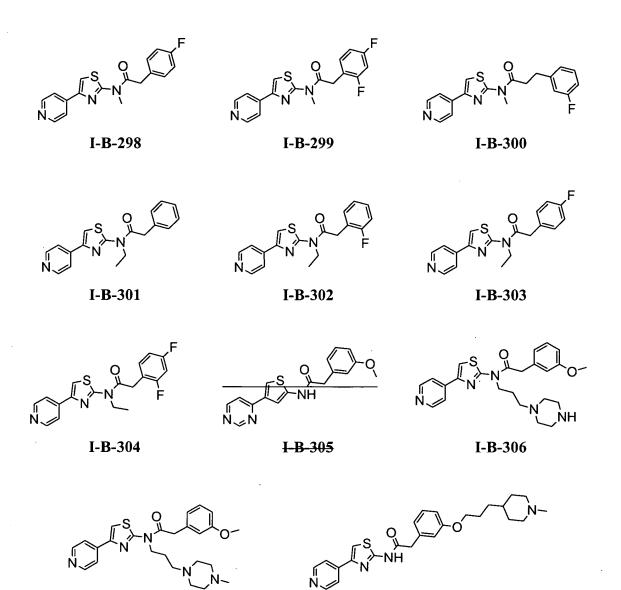
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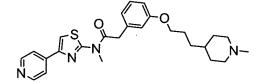
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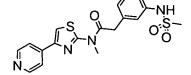
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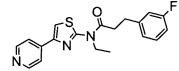
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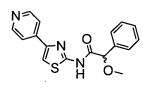
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$$I-C-34$$

$$I-C-36$$

$$I-C-36$$

$$I-C-37$$

$$I-C-38$$

$$I-C-39$$

46. (Original) A composition comprising an effective amount of compound of claim 1, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

47-53. (Canceled)

54. (Previously presented) A method of treating or lessening the severity of a disease or disorder selected from Alzheimer's disease, an allergy, asthma, or diabetes in a patient,

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said method comprising administering to said patient a compound or a composition comprising a compound having the formula:

$$\begin{bmatrix} R^1 \\ N & Z^1 \\ Z^2 & Z^3 \end{bmatrix} \xrightarrow{R^2} R^2$$

or a pharmaceutically acceptable salt thereof, wherein:

R¹ is halogen, CN, NO₂, or V_mR;

 Z^1 and Z^3 are each independently CR^Z , and Z^2 is CR^1 ; each occurrence of R^Z is independently halogen, CN, NO_2 , or U_nR^2 ; R^2 is U_nR^2 ;

 X^1 and X^2 are each independently CR^4 or N; each occurrence of R^4 is independently halogen, CN, NO_2 , or V_mR ;

each occurrence of U or V is independently an optionally substituted C_{1-6} alkylidene chain, wherein up to two methylene units of the chain are optionally and independently replaced by -NR-, -S-, -O-, -CS-, $-CO_2$ -, -OCO-, -CO-, -COCO-, -CONR-, -NRCO-, $-NRCO_2$ -, $-SO_2NR$ -, $-NRSO_2$ -, -CONRNR-, -NRCONR-, -OCONR-, -NRNR-, $-NRSO_2NR$ -, -SO-, or $-SO_2$ -;

m and n are each independently 0 or 1;

each occurrence of R is independently hydrogen or an optionally substituted C_{1-6} aliphatic group; and each occurrence of R is independently hydrogen or an optionally substituted C_{1-6} aliphatic group, a 3-8-membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully

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unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or R and R', two occurrences of R, or two occurrences of R', are taken together with the atom(s) to which they are bound to form an optionally substituted 3-12 membered saturated, partially unsaturated, or fully unsaturated monocyclic or bicyclic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

 Q^1 is -CO-, -SO₂-, or -SO₂NR-;

 R^3 is Q^2 -Ar¹,

or R² and Q¹-R³, taken together with the nitrogen atom, form the cyclic group:

55² N Q³ Ar²

, where s is 1 or 2, each occurrence of Y is independently, as valency and stability permit, -CO-, -CS-, -SO₂-, -O-, -S-, -NR⁵-, or -C(R⁵)₂-, and R⁵ is U_nR ';

 Q^2 and Q^3 are each independently a bond or a C_{1-6} alkylidene chain, wherein up to two methylene units of the chain are each optionally and independently replaced by -S-, -O-, -CS-, -CO₂-, -OCO-, -CO-, -COCO-, -CONR'-, -NR'CO-, -NR'CO₂-, -SO₂NR'-, -NR'SO₂-, -CONR'NR'-, -NR'CONR'-, -OCONR'-, -NR'NR'-, -NR'SO₂NR'-, -SO-, or -SO₂-; and wherein any carbon atom in the one or more methylene units is optionally substituted with one or two occurrences of R^6 , wherein each occurrence of R^6 is independently halogen, CN, NO₂, or U_nR', or two occurrences of R^6 , or R' and R^6 , taken together with the atoms to which they are bound, form an optionally substituted 3-6-membered cycloalkyl, heterocyclyl, aryl or heteroaryl ring; [[and]]

Ar¹ is a 5-8 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from oxygen or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from oxygen or sulfur; wherein Ar¹ is optionally substituted with 0-5 independent occurrences of TR⁷; wherein T is a

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bond or is a C_1 - C_6 alkylidene chain wherein up to two methylene units of T are optionally and independently replaced by -NR-, -S-, -O-, -CS-, $-CO_2$ -, -OCO-, -CO-, -CO-, -CO-, -CO-, -CO-, -CO-, -CO-, -CO-, $-NRCO_2$ -, $-SO_2$ NR-, $-NRSO_2$ -, -CONRNR-, $-NRSO_2$ NR-, -SO-, or $-SO_2$ -;

Ar² is a 5-8 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; wherein Ar² is optionally substituted with 0-5 independent occurrences of TR⁷; wherein T is a bond or is a C₁-C₆ alkylidene chain wherein up to two methylene units of T are optionally and independently replaced by –NR-, -S-, -O-, -CS-, -CO₂-, -OCO-, -CO-, -COCO-, -COCO-, -NRCO₂-, -SO₂NR-, -NRSO₂-, -CONRNR-, -NRCONR-, -NRNR-, -NRSO₂NR-, -SO-, or -SO₂-; and each occurrence of R⁷ is independently R', halogen, NO₂, or CN.

- 55. (Previously presented) The method of claim 54, wherein said compound or composition is used to treat or lessen the severity of an allergy or asthma.
- 56. (Previously presented) The method of claim 54, wherein said compound or composition is used to treat or lessen the severity of diabetes.